(b) contacting said first stage reaction product with at least one other [UT116] oligonucleotide to obtain a second stage reaction product, with the proviso that the other [UT116] oligonucleotide is located 3' to the [UT116] oligonucleotides utilized in step (a) and is complementary to said first stage reaction product; and

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(c) detecting said second stage reaction product as an indication of the presence of the target [UT116] polynucleotide, wherein the [UT116] oligonucleotides utilized in steps (a) and (b) have at least [50%] 70% identity with a sequence selected from the group consisting of SEQUENCE ID NOS 1-12, and [fragments or] full complements thereof.

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17. (Amended) The method of claim 1, wherein the presence of said target [UT116] polynucleotide in said test sample is indicative of urinary tract disease.

REMARKS

Claims 1-9 and 17-19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial or credible asserted utility or a well established utility. The Examiner states that absent any characterization of the UT116 product and the significance of its distribution, the detection of a UT116 product is not a substantial utility.

Applicant vigorously disagrees. UT 116 is a novel polynucleotide which is found in 78.5% of urinary tract tissue libraries and in only 4.2% of other non-urinary tract tissue libraries. Thus, it is 18 times more abundant in the urinary tract than the rest of the body based on its quantitative occurrence in a series of expressed sequence tags (ESTs) compiled as an EST database . (Data obtained from Incyte Pharmaceutical's Lifeseq database). As is known scientists skilled in the cancer diagnostic arts, a gene product, such as a protein or messenger RNA (mRNA) coding for the protein, which is more prevalent and specific to one tissue type than other tissue types, is extremely useful as a marker for the detection of disease in that tissue. If a protein appears in a tissue or body compartment where its normal occurrence is very low or non-existent, then the specific tissue in which the protein is normally found is in a diseased state. This is because the disease causes an alteration to the protein-specific tissue resulting in the protein escaping from its normal tissue into another. There are three main conditions which cause a tissue-

specific protein to exist outside its specific host tissue: massive trauma, ischemia and hypertrophic proliferation. Thus, if a patient has not experienced a massive trauma or ischemia, detection of a tissue-specific protein outside that protein's host tissue indicates that the precise disease is hypertrophic proliferation of that tissue, the most serious form being cancer. There are many examples of the diagnostic use of tissue-specific protein markers . For instance, the appearance of prostate specific antigen (PSA) in the prostate and seminal plasma is normal, but its detection in blood is indicative of prostate cancer. Further, the appearance of PSA messenger RNA (mRNA) in blood is indicative of prostate cancer. Likewise, the appearance of carcinoembryonic antigen (CEA) in colon and stool is normal, but its detection in blood at elevated levels is indicative of colorectal cancer. Thus, the appearance of UT 116 protein or mRNA in a patient blood sample is indicative of urinary disease.

Subsequently, it has been found that UT116 is identical to PSCA (prostate stem cell antigen) which has been strongly linked to prostate cancer. (see attached Exhibit A) The closest known relative to UT116 besides the identical PSCA is SCA2, normally found in gallus gallus (chicken). The strong homolgy (i.e. resemblence with conserved cysteine's for disulfide bond conservation) between SCA2 and UT116 is remarkable given the species difference. SCA2 is a cell surface marker which, like PSCA, is cancer-related. In the attached paper (Exhibit B), SCA2 is shown to be up-regulated when a normal cell is transformed to a malignant cell in a model for malignant transformation.

Not only is the homolgy of UT 116 with PSCA and SCA2 indicative of UT116's utility as a cancer marker, but it is also linked to the cell membrane via a glycosylphosphatidylinositol (GPI) anchor, the same as PSCA and SCA2. One of the classic tumor markers, CEA, is also GPI linked to the membrane of cells which express it. This evidence, i.e. the strong homology with known cancer markers and GPI linkages, coupled with UT 116's specificity to urinary tract tissue further illustrate UT116 utility as a urinary tumor marker

Claims 1-9 and 17-19 are rejected under 35 U.S.C. 112, first paragraph. The Examiner states that there is no evidence that at the time of filing the applicant was in possession of a representative sampling of fragments that are at least 50% identical to fragments of SEQ ID NO: 1-12.

Thus, in an effort to expedite prosecution, Applicant has raised the percent identity and deleted the "fragment" language from the claims and it is respectfully requested that this rejection be withdrawn.

Claims 17-19 are rejected under 35 U.S.C. 112, first paragraph. The Examiner states that one of skill in the art can not practice the claimed invention, with the broadly claimed probes and primers, with a reasonable expectation of success, the detection of urinary tract disease, without undue additional experimentation.

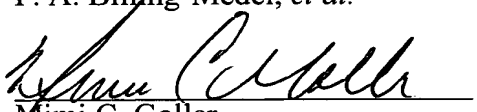
Again, based on the amendments to the claims which delete "fragment" language and raise the percent identity, it is respectfully requested that this rejection be withdrawn.

CONCLUSION

In view of the aforementioned amendments and remarks, the aforementioned application is in condition for allowance and Applicant requests that the Examiner withdraw all outstanding objections and rejections and to pass this application to allowance.

Respectfully

P. A. Billing-Medel, *et al.*



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